Together, we can explore options that may help improve Long COVID symptoms

RECOVER SLEEP

COMPLEX SLEEP DISTURBANCES GROUP

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Welcome to RECOVER-SLEEP

About This Study

RECOVER-SLEEP is studying interventions, or possible treatments, for people who have sleep disturbances related to Long COVID. Sleep disturbances may include problems falling or staying asleep, feeling very tired during the day, or problems with the sleep-wake schedule.

Researchers want to better understand how the virus that causes COVID affects sleep and find possible treatments to improve sleep quality and daily functioning for people who have Long COVID. This study will enroll adults who have sleep problems or whose sleep problems have gotten worse as a result of Long COVID and who have not had another COVID infection in the past 4 weeks.

After completing a sleep evaluation, participants will be assigned to one of the following study groups that best matches the type of sleep disturbance they are experiencing:

Hypersomnia

- sleeping longer than usual or feeling very sleepy or tired during the day, even after uninterrupted sleep at night

Complex PASC-Related Sleep Disturbances (CPSD) that may include:

- problems falling or staying asleep
- poor-quality sleep
- an irregular sleep-wake schedule

The information in this brochure describes what participants in the Complex Sleep Disturbances group can expect as part of the RECOVER-SLEEP trial. Study interventions include behavioral sleep therapy, melatonin, and light.

Why Your Participation Matters

More than 500 million people around the world have had COVID, and it's possible that millions of them could have long-term symptoms. We need more information to support the safe use of potential treatments for people with Long COVID.

With your help, we can better understand why and how Long COVID affects people's sleep and explore ways to treat sleep disturbances associated with Long COVID. This research may help you, your loved ones, and other people with Long COVID.

What to Expect in the Complex Sleep Disturbances Group

Length of Study	Study Visits	Study Interventions	Follow-up
Participate in the study for 13 weeks (about 3 months)	Visit the study clinic 2 times	Complete behavioral sleep therapy and other study interventions, provided at no cost	Answer follow-up questions about your health and well-being

About the Study Interventions

During the 8-week study intervention period, all participants will receive:
individualized behavioral study education to help participants develop healthy habits to regulate their sleep-wake patterns and improve their quality of sleep

RESET-PASC focuses on 4 things:

1. Matching the time spent in bed to actual time sleeping.
2. Waking up at the same time every morning and going to bed at the same time every night, regardless of how long you sleep.
3. Going to bed and waking up according to a schedule that best fits your lifestyle needs.
4. Keeping naps brief and early in the day.

Study activities for RESET-PASC include:

- Learning about what you need to do to help improve your sleep
- Creating a plan to help you sleep
- Finding ways to improve your sleep
- Developing a plan for how to handle future sleep difficulties

The study team will work with you to schedule your individual RESET-PASC video sessions during the study intervention period. These video sessions include:

Assessment Session (30-45 minutes)	Intervention Session (30-45 minutes)	Check-in Session (15 minutes)	Check-in Session (15 minutes)	Summary/ Continued Care Plan Session (35 minutes)

These video sessions will be led by study staff who are trained in RESET-PASC.

By participating in this study intervention, you will help the study team learn if RESET-PASC can help:

- Optimize your sleep quality, amount, regularity, and timing
- Manage excessive daytime sleepiness or napping
- Enhance the effectiveness of the other study interventions described in the next section

In addition to RESET-PASC, you will be assigned by chance to one of these groups:			
Active Melatonin + High-intensity Light	**Active Melatonin + Low-intensity Light**	**Placebo Melatonin + High-intensity Light**	**Placebo Melatonin + Low-intensity Light**

In this study, melatonin and the placebo are both referred to as study drugs.

- **Melatonin** (pronounced mel-uh-TOW-nen) a natural hormone in the brain that helps regulate the timing of sleep, given to participants as a supplement pill. It is taken by mouth every evening 2 hours before bedtime.
- **Placebo melatonin** looks like the melatonin pill but has no active ingredients and should have no effect. It is also taken by mouth every evening 2 hours before bedtime.

- **High-intensity Light** is noninvasive exposure to a bright light that may help improve and regulate sleep-wake patterns.
- **Low-intensity Light** looks like the high-intensity light and is unlikely to influence sleep-wake patterns.

If you receive a placebo as part of this study, your symptoms of sleep disturbances may not improve or may get worse. You, your study doctor, and the study team will not know if you are receiving melatonin or placebo melatonin or high-intensity or low-intensity light, but they can quickly find out if needed for your safety or well-being.

Important Reminders about Pregnancy and Breastfeeding

- The effects of the study drug on a developing pregnancy or a breastfeeding infant are unknown. If you are pregnant or breastfeeding, you should not take part in this study.
- If you could become pregnant and you have a sexual partner who is able to have children, **you must use an effective method of birth control** to avoid becoming pregnant during the study and for at least 7 days after finishing the study drug due to potential side effects of the study drug.
- If you have questions about what is considered effective birth control, please ask the study team.

About Melatonin and Light

You will receive the following study interventions to use at home during the study.

Wearable Light Sensor

What you will receive

- A wireless light sensor you can wear as a pendant around your neck.

How it works

- The light sensor will measure the light in your environment while you are wearing it.
- This light sensor will help the study team learn about the amount of light you are exposed to during the study intervention period.

Instructions for Use

- Wear the light sensor while awake for 7 days before starting any of the other study interventions.
- Wear the light sensor while awake for the last 7 days of the 8-week study intervention period.
- Avoid all exposure to lighting 1 hour before your desired bedtime. This includes lighting from electronics and daylight.
- Return the light sensor at the end of the study intervention period.

Optional (and recommended):

- Wear the light sensor throughout the entire study.

Melatonin (active or placebo)

What you will receive

- A pill bottle with enough of the study drug to last 10 weeks. The melatonin in this study is a 3 mg immediate release pill.

Important information

- Store the study drug at room temperature (68°F to 77°F).
- Keep it away from heat, moisture, and light.
- Do not freeze the study drug.

Instructions for Use

- Take 1 pill by mouth daily 2 hours before your desired bedtime (when you will try to fall asleep) for 8 weeks.
- Return any extra study drug pills at the End of Intervention Clinic visit.

Light (high-intensity or low-intensity)

What you will receive

- A table lamp
- Two light bulbs
- Timer

How it works

- A **table lamp** and **light bulbs** will deliver white light to your open eyes. The study team will be in touch with you the week before starting the study intervention and will guide you in setting up the table lamp in your home.
- The light has a **timer** that will be set to turn on at your desired wakeup time. It will turn off 4 hours before your desired bedtime.
- The **table lamp** must be plugged into an electrical outlet in the room where you spend most of your time, especially your mornings.

Instructions for Use

- Use your table lamp within 2 hours of waking for at least 1 hour for 8 weeks. You can perform any tasks (reading, eating, watching TV) while sitting next to your table lamp, but make sure you have your eyes open during this time.
- The table lamp should be no more than 18 inches away from your face.
- If you choose to do so, you can use the table lamp for more than 1 hour during daytime hours (between 6 a.m. and 6 p.m.) for 8 weeks.
- You may keep the table lamp after the study ends.

At the beginning of the study, you will also receive:

Activity Tracker

- During the study intervention period, you will be asked to wear an activity tracker on your wrist, similar to a watch, to record rest and activity patterns.
- Please wear the activity tracker for 7 days before you start taking the study drug and for the last 7 days you are taking the study drug (14 days total).
- You are encouraged to wear the activity tracker for the duration of the study.
- The study team will help you set up the activity tracker and app. Your activity tracker will need to be connected to WiFi once a day to transmit the data. You will also need to download an app to a mobile device.
- You may keep the activity tracker for personal health monitoring after the study ends.

Sleep Diary (online or paper format)

- A sleep diary is a record of your rating of the quality of your sleep.
- You will be asked to complete the sleep diary for 7 days before you start taking the study drug and for the last 7 days you are taking the study drug (14 days total).
- This information will help researchers understand how the study interventions affect participants' day-to-day sleep patterns and sleep quality.

RECOVER-SLEEP: Complex Sleep Disturbances Participant Schedule

This schedule summarizes the study activities for participants assigned to the Complex Sleep Disturbances group. You will complete the study interventions and activities listed here.

STUDY ACTIVITIES: 13 Weeks (About 3 Months Total)

Screening and Baseline Period: 1 Week

Screening assessments will take about 5 hours

	Information	Assessments	Receive
Randomization Visit (about 3 to 5 hours) **Date: _____** Some of the activities are phone and internet-based and can be completed at home.	• Review current medicines • Review study requirements • After this visit, complete a survey about how you are feeling	• Surveys • Sleep symptoms and habits • Attention and thinking speed test • Blood sample • Nasal swab sample • Check-in • Pregnancy test, if applicable	• Study drug • Wearable light sensor • Activity tracker • Table lamp • Light bulbs • Timer • Information on brief behavioral treatment (RESET-PASC) • At-home stool (poop) sample kit • Sleep Diary (if using paper format)

Pre-Study Intervention Period: 1 Week

From _____
to _____

- Have a phone call that will last around 1 hour with a study team member who will guide you in setting up the light sensor, table lamp, light bulbs, and timer.

For 7 days before you begin the study interventions at home

- Wear the light sensor to record your exposure to light
- Wear the activity tracker to record your rest and activity
- Fill out Sleep Diary 1 (online or on paper) to record the time you spent sleeping and napping and the quality of your sleep
- Discuss your desired sleep-wake schedule with trained study staff

Study Intervention Period: 8 Weeks (2 Months)

Complete Study Intervention

From _____
to _____

- Take the study drug by mouth daily
- Use the table lamp with light bulbs daily
- Complete brief behavioral treatment (RESET-PASC) video sessions with trained study staff, as scheduled. Each session will last around 30 minutes.
- Wear the light sensor and activity tracker daily (recommended, but not required)

Middle of Study Intervention Phone Call (about 30 to 60 minutes)

Date: _____

Between week 3 and week 6, the study team will call you for another check-in.

<table>
<tr><td>Pre-End of Study Intervention Period

From _____
to _____</td><td colspan="3">For the last 7 days of the study intervention period
Wear the light sensor to record your exposure to light
Wear the activity tracker to record your rest and activity
Fill out Sleep Diary 2 (online or on paper) to record the time you spent sleeping and napping and the quality of your sleep</td></tr>
<tr><td rowspan="2">End of Study Intervention Clinic Visit (about 2 to 4 hours)

Date: _____</td><td>Information</td><td>Assessments</td><td>Receive / Return</td></tr>
<tr><td>Review current medicines
After this visit, complete a survey about how you are feeling</td><td>Study drug pill count
Surveys
Sleep symptoms and habits
Attention and thinking speed test
Blood sample
Check-in</td><td>Receive
At-home stool (poop) sample kit
Return
Remaining study drug, if applicable
Wearable light sensor
Completed Sleep Diary (if using paper format)</td></tr>
<tr><td colspan="4">End of Study: 4 Weeks (1 Month) Later</td></tr>
<tr><td>End of Study Follow-up Phone Call (about 30 to 60 minutes)

Date: _____</td><td colspan="3">A study team member will call you for a check-in about 4 weeks after you finish the study interventions. During this call, we will ask if you have any new or worsening symptoms.</td></tr>
</table>

Notes

About the RECOVER Research Biorepository

The RECOVER Research Biorepository is designed to collect and store biospecimens for future research related to the RECOVER Initiative. Biospecimens may include samples of blood, stool (poop), and nasal swabs. These samples will be stored securely until they are used up.

Participating in this study means you agree to share your data and biospecimens with the RECOVER Research Biorepository. **If you choose to participate in this study, your data and samples may also be shared with other researchers for future research, such as developing new tests and treatments for Long COVID or other health problems**. You can change your mind later, but researchers might still use your data and biospecimens if they have already been shared and we are not able to link your samples back to you because they have already been de-identified.

Why is a biorepository needed?

Biospecimens from a blood sample can provide valuable information to researchers. This information is called a "biomarker." For example, a person's blood sugar level is one of the biomarkers for diabetes. Biomarkers can be measured and may provide important information about Long COVID. They may also predict how a patient will respond to a treatment.

How could a biorepository help with Long COVID research?

Sharing your data and biospecimens with the RECOVER Research Biorepository may:

- Increase the possibility of developing new interventions and possible treatments related to Long COVID
- Improve our understanding of how antiviral drugs and other interventions may work to reduce Long COVID symptoms
- Enhance our understanding of how and why Long COVID affects people differently
- Help researchers make important discoveries and uncover possible therapies that could help your family and others in the future

How will my privacy be protected?

Your data and samples will be de-identified, which means they will not include any information that can personally identify you, and researchers cannot easily link your identifying information to the data and samples.

What will the samples be used for?

RECOVER research
The samples will be used for research on COVID and the long-term effects of the virus that causes COVID-19. They may also be used for research on other health problems.

Genetic testing (optional)
The use of your samples for genetic testing is optional, and you can let the study team know your decision in the Informed Consent Form. If you give your permission, researchers may study your genes to look for links to Long COVID. Genetic tests can determine if a person or groups of people are more likely to have certain genetic diseases or conditions. Choosing to say no to genetic testing will not limit your ability to participate in other parts of this study, including using the study interventions.

Will I get any results back from future research use of my data and biospecimens?

No. You should not expect to receive results from any future research that may use your data and biospecimens.

Blood Samples

When will I have blood drawn for the biorepository?
The study team will take about 5 tablespoons (80 ml) of blood from your arm during specified study visits.

Stool Samples

How will I provide stool samples?
After the Baseline and End of Study Intervention visits, you will be asked to provide a stool (poop) sample using an at-home kit. The at-home kit will include a confidential pre-paid box for you to mail your sample directly to the RECOVER Research Biorepository where it will be stored securely.

Why are stool samples important to this research?
People who have had COVID can have changes in their microbiome (microorganisms like fungi, bacteria, and viruses that live in the intestines) in their stool after their infection. Collecting stool samples helps researchers understand changes in the microbiome caused by the COVID-19 infection.

If You Become Ill or Injured
Get the medical care that you need right away. Visit your doctor, go to urgent care, or go to the emergency room if needed.

Contact Your Study Team if You
- Start taking any new medicines
- Change your phone number, email, or home address
- Have questions about the study or the study drug
- Experience new or worsening symptoms
- Receive emergency medical care or are hospitalized
- Become pregnant or think you could be pregnant

Site Contact Information

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For more information and study updates, visit trials.recovercovid.org/sleep

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